An in vivo photodynamic therapy with diode laser to cell activation of kidney dysfunction

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An in vivo photodynamic therapy with diode laser to cell activation of kidney dysfunction

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Abstract. This study aims to analyze the effect of photodynamic therapy (PDT) low level laser therapy (LLLT) 650 nm in the experimental animals mice (*Musmuculus*) suffering from kidney organ damage in mice (*Musmuculus*) in vivo. Exposure laser acupuncture was performed on the kidney BL-23. The conditioning of kidney damage in mice used carbofuraan 35 at a dose of 0.041697 mg/mice. LLLT 650 nm exposure was done on a wide variety of energy (0.5; 1.0; 1.5; 2.0; 4.0; 5.0; 6.0; 7.0) J. The histopathological kidney cells in mice renal impairment showed that exposure to 650 nm laser energy 1 Joule resulted in the reduction of damaged cells (necrosis) and normal cells were increased with the improvement of renal tubular cells (64.14 ± 8:02)%. Therefore, exposure to 650 nm LLLT on acupuncture points Shenshu (BL-23) has the ability to proliferation of renal tubular cells of mice.

1. Introduction

Since 2008, biostimulation laser, which is now referred to as Low Level Laser Therapy (LLLT), has been applied to medical therapy [1]. He-Ne laser is the first laser used for wound healing. Biostimulation laser is a photobiology phenomenon that involves chemical reactions and enzymes [2]. Photodynamic activation for biostimulation cells using LLLT is laser stimulation of the skin with low intensity and a non-thermal laser irradiation. Deep transmission of laser energy, wavelength, and laser energy are the important factors on therapy. In additional, scattering and absorption by various tissues of different skins need to be considered. The skin is a network of multi-layer in a homogeneous, anisotropic structure; so that the optical properties are very complex [3]. The intensity of light through the skin decreases exponentially due to the scattering and the absorption. Ultraviolet and visible spectrum (~400-600) nm will be absorbed by hemoglobin and melanin, so, a little amount of the light is transmitted back. For blue light, the irradiance depth would be decreased 99% to ~700 μm. Wavelengths above 1400 nm is the area of water absorption that results on less transmission. Red and infrared spectrum are the most widely used for photodynamic biomodulation because the absorption is very small and the transmission is large [4]. However, scattering by collagen is still considered because it could reduce transmission.

Kidney Disease Outcomes Quality Initiative of The National Kidney Foundation defines that chronic renal failure is a state of the occurrence of kidney damage or glomerular filtration rate (GFR) <60 mL/min/1.73 m^2 within 3 months or more [5]. The disorder is caused by dysfunction of the

glomerular filter or blood and protein filter in the primary urine. Generally, dialysis or hemodialysis could be upgraded to kidney transplant in order to treat chronic kidney failure. Alternative therapy to restore organ function is photodynamic activation through photobiomodulation of kidney cells with a laser exposure. This laser exposure can be performed on acupuncture points, which also called Laserpunktur therapy [6]. Laser therapy acupuncture has many advantages. It is non-invasive, free cause of infection, and environment-friendly. It does not cause pain because of its needle pricks, reduces the risk of disease transferred through a needle, and radiates warm feelings during the therapy. Furthermore, it also causes high immune system response, high growth factor, and is safe for all ages [7]. Based on research, specific acupuncture points used for kidney treatment is shensu (BL-23) [8]. This paper discusses the influence of laser phototherapy at 650 nm in testing animals, which are mice (*Musmuculus*) suffered from kidney disorders, on the kidney acupuncture points BL-23.

2. Materials and methods

Animals used in this study were mice (*Musmusculus*), male, 3-4 week old, and weighing 25-35 grams. *Musmuculus* were conditioned with damaged kidney by giving carbofuran 3% on the dosage of 0.5 mg/kg weight *Musmuculus* [9]. LD_{50} fraction did not cause the death of the tested animals, yet caused kidney damage is 1/24 LD_{50} (0.0208 mg / kg), 1/12 LD_{50} (0.0417 mg/kg) and 1/6 LD_{50} (0.0833 mg/kg). Therefore, kidney of mice (*Musmusculus*) were set to damaged condition by using Carbofuran 3% with a dose of 0.041697 mg/mice.

2.1. Light sources

Laser irradiation was carried out using diode lasers with output wavelengths of (650.00±0.01) nm. The power outputs were (16.53 ± 0,06) mW. Those data were the result of characterization using Jasco monochromator CT-10 and OPM (Optical Power Meter) Thorlabs PM100D which were capable of detecting power between 100 pW – 200 W and a wavelength of 185 nm – 25 μm. The laser energy was calculated from the output power multiplied by the length of time the laser exposure [11].

2.2. Laser treatment

To determine the laser effect on *Musmuculus*, the samples were distributed into 3 groups, as follows: (1) Groups A was treated using carbofuran and laser 405 nm (C+L+), (2) Groups B was treated only with carbofuran (C+L-), and (3) Group C had no treatment of everything (C-L-). For each group the experiment was repeated at least 3 times. Group A was treated with various energy irradiating of diode laser (1.0; 1.5; 2.0; 4.0; 5.0; 6.0; 7.0) J to acupuncture point kidney (BL-23). Figure 1 shows the acupunctured point BL-23.

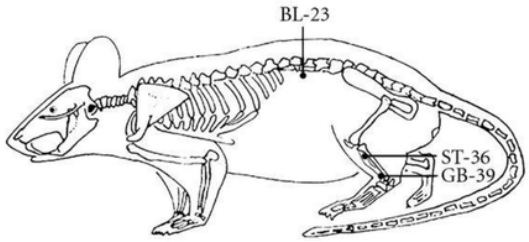


Figure 1. Accupuncture point of kidney BL-23

2.3. Histopathological anatomy test

Histopathology test was used to determine the structure of the cells of the renal tubules of mice that had been given laser irradiation treatments as well as healthy and pain control. Analytical calculation of renal tubular cell was conducted using a visual field [10]. The formula to calculate the percentage of regenerated normal cell is by using equation:

$$\%\ \text{of normal tubular cells} = \frac{\bar{x}\ \text{control diseased cells} - \bar{x}\ \text{number of normal cells}}{\bar{x}\ \text{control diseased cells}} \times 100\%$$

3. Results and discussion

Laser characterization results in this study are showed in Figure 2 and 3.

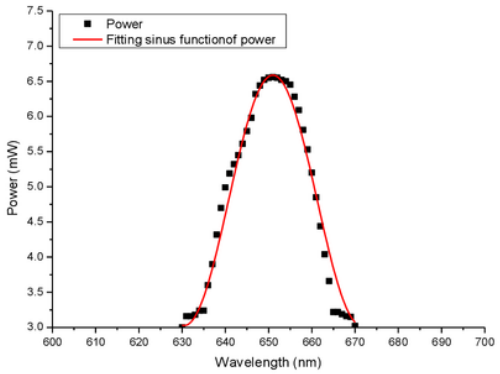


Figure 2. Spectrum of 650 nm diode laser

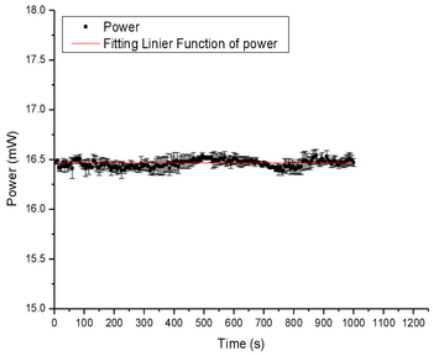


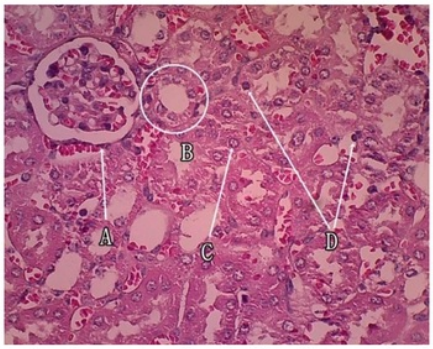
Figure 3. Graph of 650 nm laser power stability versus time

The characterization results in Figure 2 show that the diode laser light source has a spectrum (650.00 ± 0.01) in nm. Figure 3 shows the data output on power stability (16.53 ± 0.06) mW

3.1 Histopathological analysis results

Giving carbofuran orally in mice resulted in infiltration of inflammatory cells and necrosis in renal cells which are indicated by damage within kidney cells [10]. Necrosis is the death of cells in living tissue due to the toxins which enter the body. Inflammation is a complex biological response of vascular tissues to harmful stimuli, such as pathogenic agents, cell death/damaged, or irritation. Inflammation is the body armor attempting to deal with adverse stimuli and to initiate the healing process [12].

In this study, to stimulate the healing process of renal cell, the therapy applied 650 nm laser diode. This therapy was examined through seven variation of energy dose with considerably similar laser beam output because the laser mounted on Shensu acupuncture point and BL-23 had the same cross-sectional area. Figure 4a to 4f illustrate histopathological picture of *Musmusculus*' kidney glomerulus for normal cells, diseased cells, and cells that were exposed to a laser with a magnification of 400X.

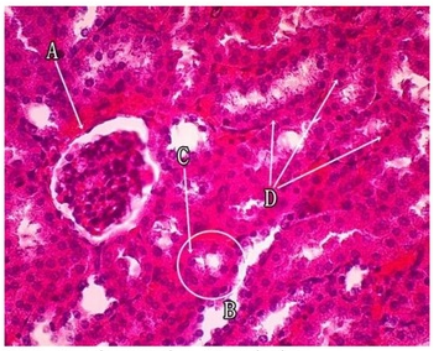


Exp: A=glomerular, B=tubulus, C=normal cell, D=Necrosis

Figure 4a. Histophatology normal kidney cells

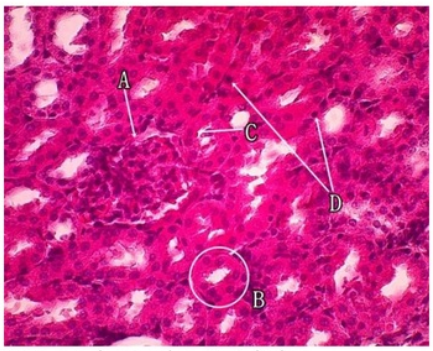
Exp: A=glomerular, B=tubulus,C=normal cell, D=Necrosis, E=Inflamed cell

Figure 4b. Histophatology disease kidney cells



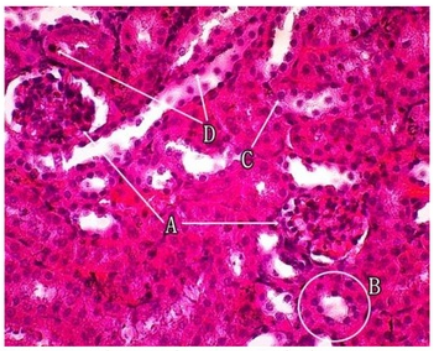
Exp: A=glomerular, B=tubulus, C=normal cell, D=Necrosis

Figure 4c.Histophatology kidney cells with treatment laser 650 nm 0.5 J



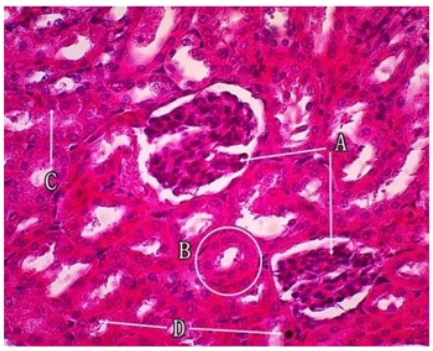
Exp: A=glomerular, B=tubulus, C=normal cell, D=Necrosis

Figure 4d. Histophatology kidney cells with treatment laser 650 nm 1.0 J



Exp: A= glomerulus, B = Tubulus, C = normal cell, D = Necrosis

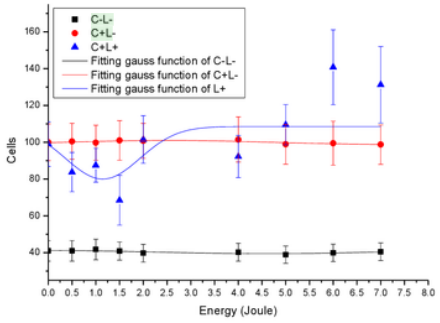
Figure 4e. Histophatology kidney cells with treatment laser 650 nm 1.5 J



Exp: A= glomerulus, B = Tubulus, C = Normal cell, D = Necrosis

Figure 4f. Histophatology kidney cells with treatment laser 650 nm 2.0 J

Figures 5a and 5b demonstrate the graph of the number of normal cells and damaged at various laser exposure.



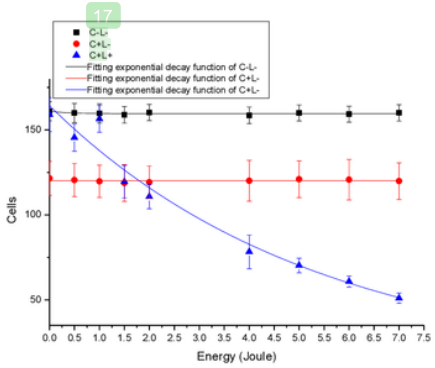


Figure 5a. The effect of various energy laser exposure on the number of damaged renal cells in mice

Figure 5b. The effect of various energy laser exposure on the number of normal cells in mice

Note:
C+L+ treated with carbofuran and laser 650 nm
C+L- treated with carbofuran and no laser treatment
C-L- no treatment laser and carbofuran

Figure 5a shows the increase in the number of normal renal cells of mice as a Gaussian function caused by exposure to 650 nm laser for various energy. The laser exposure of 650 nm wavelength and 1.5 J energy dose at acupuncture point BL-23 determines a decrease in the damaged cells the most. As indicated by the Gaussian function, $y = y_0 + \frac{A}{w\sqrt{\pi/2}} e^{-2\frac{(x-x_c)^2}{w^2}}$.

Meanwhile, the number of normal cells in the kidneys of diabetic mice as a result of exposure to 650 nm laser decreases exponentially compared to the number of normal cells if exposed toward the laser with precisely1.0 J energy. The exponential function is $y = y_0 + A_1 e^{-x/t_1} + A_2 e^{-x/t_2}$ with R^2 value of 0.96.

Figure 6 describes the percentage of renal cell improvement based on histopathological picture.

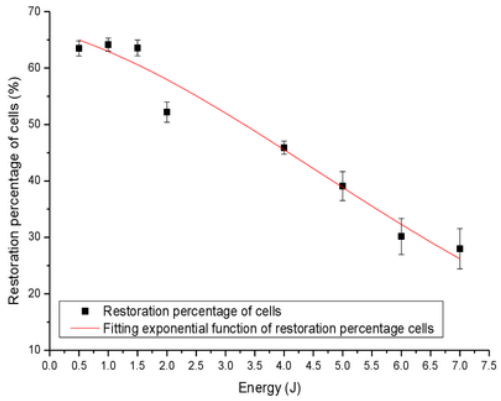


Figure 6. Growth percentage of renal tubular cells

Figure 6 figures out that the use of a 650 nm laser with 1 Joule energy has improved its percentage (64.14 ± 8.02)%, which is the most optimum result in the improvement of renal tubular cells. The exponential function is $y = y_0 + A_1 e^{-x/t_1} + A_2 e^{-x/t_2}$ with R^2 value of 0.93.

The results of this study showed that a low power laser (LLLT) at a wavelength of 650 nm with 1 J energy at acupuncture points shenshu (BL-23) had the ability to improve renal tubular cells. This is consistent with Peplow's research that shows that LLLT is able to modulate cell proliferation [13, 14]. The results also showed biomodulation effects of LLLT in myofibroblast T and B cells during wound healing. LLLT facilitates differentiation myofibroblastic during the early stages of the cicatricialrepair process. Additionally, LLLT also appears to modulate the inflammatory response by down regulating lymphocyte proliferation during the wound healing process [15].

Wavelength laser parameters also affect the ability of cell proliferation. Laser wavelength associated with the depth of penetration into skin. Some research show that wavelength affects on the biological response of HeLa cells, which are irradiated with light of 580-860 nm [16]. Results of other studies also demonstrate the use of laser 780 nm is not as effective as 660 nm laser, yet it has a positive effect on the early stages of the emergence and development of inflammation. At the end of the experimental period, major effect is seen on the amount and quality of granulation tissue. If laser 660 nm is applied daily, it will be more effective than the 780 nm laser to improve third-degree burnt healing in diabetic rats started in the early stages of post-combustion [17-18].

Senshu acupuncture points (BL-23) is a bladder meridian acupuncture points related to the kidney [19]. The bladder is associated with the internal and external kidneys. Stimulation of the points BL-23 provides strengthening effect on the kidneys and kidney bioenergy balance, which in turn will restore kidney function.

4. Conclusion

Based on the results of histopathological kidney cells in mice with renal impairment, it can be concluded that exposure to 650 nm laser with 1 J energy results in a reduction of damaged cells (necrosis) and increase of normal cells with the improvement of renal tubular cells (64.14 ± 8.02)%. Therefore, the exposure to 650 nm LLLT on acupuncture points Shenshu (BL-23) has the ability to proliferation of renal tubular cells of mice.

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